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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/594,641 | 03/28/2008 | Yousef Al-Abed | 50425/262 | 1663 |

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AMSTER, ROTHSTEIN & EBENSTEIN LLP
90 PARK AVENUE
NEW YORK, NY 10016

| EXAMINER | |
|---|---|
| EWOLDT, GERALD R | |
| ART UNIT | PAPER NUMBER |
| 1644 | |
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| 02/15/2011 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/594,641 | AL-ABED, YOUSEF | |
| | Examiner | Art Unit | |
| | G. R. Ewoldt, Ph.D. | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3,11 and 27-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,11 and 27-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

**DETAILED ACTION**

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 12/09/10 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks filed 12/09/10 have been entered.

2. Claims 1, 3, 11, 27, 28, and newly added Claims 29-33 are under examination.

3. Upon reconsideration the previous rejections under 35 U.S.C. 103(a) have been withdrawn. New rejections follow.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 3, 11, 27, and 28 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/64749 (IDS).

As set forth previously, WO 01/64749 teaches the treatment of diabetes (diabetic retinopathy) comprising administering to a human an antibody that inhibits MIF (see particularly page 32 and Claim 53). Said antibodies include monoclonal and humanized antibodies (see particularly pages 9 and 10).

The reference clearly anticipates the claimed invention.

Applicant's arguments, filed 12/09/10, have been fully considered but are not found persuasive. Applicant again argues that the reference does not teach the inhibition of the progression of type 1 diabetes. Applicant further argues that, "a prophetic treatment of diabetic retinopathy is not a teaching that an MIF antibody would inhibit the progression of type 1 diabetes in a mammal having type 1 diabetes".

The reference teaches the treatment of diabetic retinopathy, the most readily envisaged would be diabetic

retinopathy associated with type 1 diabetes. Retinopathy associated with type 1 diabetes would be the most readily envisaged because the condition is associated with long-term disturbances in the blood glucose level and since type 1 diabetes generally presents during childhood or adolescence it is a condition often seen in type 1 diabetics as they age. Treating the progression of diabetic retinopathy is encompasses by the scope of the claim reciting treating the progression of disease. Further, prophetic teachings are appropriate for use as prior art. Accordingly, the reference anticipates the claimed method.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 3, 11, 27, and newly added Claims 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bojunga et al. (2003, IDS) in view of Nishihira and Ogata (2001).

Bojunga et al. teaches the treatment of diabetes comprising the administration of a MIF inhibitor (see particularly page 185). Figure 3 of the reference further teaches that increased MIF-RNA expression precedes that onset of disease. Figure 4 of the reference teaches that from the time of MIF administration 4-10 weeks is required before the onset of disease.

The reference teaching differs from the claimed invention in that it does not teach an antibody MIF inhibitor nor the treatment of human diabetes.

Nishihira and Ogata teach the treatment of autoimmune diseases with an anti-MIF antibody and a small organic molecule and that the treatments are essentially are interchangeable (see particularly **Perspectives**). The reference further teaches that MIF is essential for T cell activation (see particularly page 778, column 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to treat diabetes, as taught by Bojunga et al., with an anti-MIF antibody because Nishihira and Ogata teach that small organic molecules are interchangeable with antibodies in the context of the treatment of autoimmune disease. The choice of either for the treatment of diabetes would not render the method patentably distinct. Regarding the treatment of humans, given that humans are the major suffers of diabetes, the treatment of humans would be obvious. Additionally, it would be obvious to treat a patient at risk of developing disease given the teachings of Bojunga et al. that, a) increased MIF-RNA expression precedes that onset of disease, and b) MIF administration precedes the onset of disease in the experiments of the reference, and c) Nishihira and Ogata teach that MIF is essential for T cell activation. Clearly T cell activation precedes disease onset (given that T cells are disease effectors) thus, it would be obvious to block the disease-causing effects of MIF as well as T cell activation before the onset of disease.

Applicant's arguments, filed 12/09/10, have been fully considered but are not found persuasive. Applicant reviews Bojunga et al. and concludes that the reference provides no data.

Applicant is advised that data is not required in prior art references.

Applicant argues that Nishihira and Ogata is not anticipatory art.

Applicant's position is acknowledged. Applicant is reminded that the rejection is for obviousness in view of the combined prior art as well as what would have been known to the ordinarily skilled artisan at the time of the invention.

8. Claims 28 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bojunga et al. (2003, IDS) in view of Nishihira and Ogata (2001), as applied to Claims 1, 3, 11, 27, and newly added Claims 29-32 above, in further view of U.S. Patent No. 5,530,101.

Bojunga et al. and Nishihira and Ogata have been discussed above.

The method of the combined references differs from the claimed method only in that it does not employ a humanized monoclonal antibody. The '101 patent, however, teaches that humanized antibodies are preferred for the treatment of humans because they are less immunogenic to humans (see particularly the Abstract). Thus, the use of a humanized anti-MIF antibody would be preferred and obvious for the treatment of human diabetes.

Applicant has not argued this rejection separately; Applicant reiterates the argument traversing the rejection of the claims in view of Bojunga et al. and Nishihira and Ogata.

See the Examiner's response in section 7, above.

9. Claims 1, 3, 11, 27, and newly added Claims 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/32606 (IDS) in view of Nishihira and Ogata (2001).

WO 01/32606 teaches the treatment or prevention of type 1 (insulin dependent) diabetes comprising the administration of a MIF inhibitor (see particularly Claim 12).

The reference teaching differs from the claimed invention in that it does not teach an antibody MIF inhibitor nor the treatment of human diabetes.

Nishihira and Ogata teach the treatment of autoimmune diseases with an anti-MIF antibody and a small organic molecule and that the treatments are essentially are interchangeable (see particularly **Perspectives**). The reference further teaches that MIF is essential for T cell activation (see particularly page 778, column 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to treat or prevent diabetes, as taught by WO 01/32606, with an anti-MIF antibody because Nishihira and Ogata teach that small organic molecules are interchangeable with antibodies in the context of the treatment of autoimmune disease. The choice of either for the treatment of diabetes would not render the method patentably distinct. Regarding the treatment of humans, given that humans are the major suffers of diabetes, the treatment of humans would be obvious. Note that "prevention" encompasses the treatment of an at risk individual.

10. Claims 28 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/32606 (IDS) in view of Nishihira and Ogata (2001), as applied to Claims 1, 3, 11, 27, and newly added Claims 29-32 above, in further view of U.S. Patent No. 5,530,101.

WO 01/32606 and Nishihira and Ogata have been discussed above.

The method of the combined references differs from the claimed method only in that it does not employ a humanized monoclonal antibody. The '101 patent, however, teaches that humanized antibodies are preferred for the treatment of humans because they are less immunogenic to humans (see particularly the Abstract). Thus, the use of a humanized anti-MIF antibody would be preferred and obvious for the treatment of human diabetes.

11. No claim is allowed.

12. Applicant has inquired as to why author's names and publication dates are required on an IDS for search reports and IPERs.

Applicant is advised that the IDS requirements set forth in MPEP 609 have not been waived for search reports and IPERs.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0841.

14. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-

free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

/G.R. Ewoldt/
G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600